8A03

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM 12-912

Requestor's Name: Geetha Bansal

Serial Number: 08/090754

Date: 12/29/98 Phone: 305-3955 Art Unit: 1642

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

Please search

Method of eliciting an Immune Response administering a comp^n comprising a complex consisting of heat shock protein bound to an antigenic molecule, where the complex is in the range 10 - 600 micrograms of hsp70, or 50 - 5000 micrograms of hsp 90 or 10 - 600 micrograms of ~~hsp~~ gp 96

2. A method of purifying hsp-70 peptide Complex binding to by a non hydrolyzable analogue of ATP column

3. A kit comprising:-
a composition of heat shock protein 70 or gp96 bound to an antigenic molecule in an amount 10 - 600 µg.

pat. 1-5

STAFF USE ONLY

Date completed: 1-6-99
Searcher: BOB x8-4291
Terminal time: 40
Elapsed time: prep 20
CPU time:
Total time:
Number of Searches:
Number of Databases: 11

Search Site
- ___ STIC
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- ___ Pre-S

Type of Search
- ___ N.A. Sequence
- ___ A.A. Sequence
- ___ Structure
- ✓ Bibliographic

Vendors
- ___ IG
- 108 STN 3
- 4540 Dialog 8
- ___ APS
- ___ Geninfo
- ___ SDC
- ___ DARC/Questel
- ___ Other

PTO-1590 (9-90)

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=> fil capl; d que l11; d que l17; d que l18; d que l23; s l11 or l17 or l18 or l23; fil
medl; d que l33; d que l35; d que l51; s l33 or l35 or l51
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FILE COVERS 1967 - 6 Jan 1999 VOL 130 ISS 2
FILE LAST UPDATED: 6 Jan 1999 (19990106/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4            895 SEA FILE=CAPLUS ABB=ON  GP96 OR GP90 OR GP70 OR GP(W)(96
                  OR 90 OR 70)
L6         987362 SEA FILE=CAPLUS ABB=ON  COMPLEX?
L8           8270 SEA FILE=CAPLUS ABB=ON  IMMUNOSTIMUL?
L11             5 SEA FILE=CAPLUS ABB=ON  L2 AND L4 AND L6 AND L8


L2          13398 SEA FILE=CAPLUS ABB=ON  HEAT SHOCK
L13        292161 SEA FILE=CAPLUS ABB=ON  COLUMN#
L16          3613 SEA FILE=CAPLUS ABB=ON  NON HYDROLY? OR NONHYDROLY?
L17             3 SEA FILE=CAPLUS ABB=ON  L13 AND L16 AND L2


L2          13398 SEA FILE=CAPLUS ABB=ON  HEAT SHOCK
L6         987362 SEA FILE=CAPLUS ABB=ON  COMPLEX?
L13        292161 SEA FILE=CAPLUS ABB=ON  COLUMN#
L16          3613 SEA FILE=CAPLUS ABB=ON  NON HYDROLY? OR NONHYDROLY?
L18             2 SEA FILE=CAPLUS ABB=ON  L2(L)L6 AND L16 AND L13


L2          13398 SEA FILE=CAPLUS ABB=ON  HEAT SHOCK
L4            895 SEA FILE=CAPLUS ABB=ON  GP96 OR GP90 OR GP70 OR GP(W)(96
                  OR 90 OR 70)
L6         987362 SEA FILE=CAPLUS ABB=ON  COMPLEX?
L19        258915 SEA FILE=CAPLUS ABB=ON  BOUND
L20         41321 SEA FILE=CAPLUS ABB=ON  ANTIGENIC?
L21            48 SEA FILE=CAPLUS ABB=ON  L2(L)(L6 OR L19)(L)L20
L23             8 SEA FILE=CAPLUS ABB=ON  L4 (L) L21


L63            12 L11 OR L17 OR L18 OR L23


FILE 'MEDLINE' ENTERED AT 10:11:08 ON 06 JAN 1999

 FILE LAST UPDATED: 29 OCT 1998 (19981029/UP). FILE COVERS 1966 TO DATE.
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Searched by Barb O'Bryen, STIC 308-4291

asthmatics, as well as the effect of low dose fluticasone propionate treatment. Methods. Twenty-three asthmatics and eight normal subjects were selected. In each subject BAL and bronchial biopsies were performed. Eighteen out of 23 asthmatics, underwent the second bronchoscopy after 6 weeks of low dose inhaled fluticasone propionate treatment (250 mug bd) in a placebo-controlled double-blind study. BAL fluid and biopsies were processed to evaluate HLA-DR and ****hsp70**** expression by immunochemistry methods. Results. ****Hsp70**** and HLA-DR upregulation was present on professional and non-professional antigen presenting cells (APCs). In asthmatics, the ****hsp70**** and HLA-DR expression was higher in BAL (****hsp70**** P < 0.001, HLA-DR P < 0.001) and bronchial epithelium (****hsp70**** P < 0.001, HLA-DR P < 0.001) when compared with controls. We also observed a significant correlation between ****hsp70**** and HLA-DR expression in BAL (P < 0.005) and epithelium (P < 0.001). Fluticasone propionate treatment down-regulated the ****hsp70**** and HLA-DR expression in BAL (****hsp70**** P < 0.001, HLA-DR P < 0.05) and bronchial epithelium (****hsp70**** P < 0.05, HLA-DR P < 0.05). A serial section comparison study showed that CDla+ cells and macrophages were positive for both ****hsp70**** and HLA-DR in the submucosa. Conclusions. Our results support the hypothesis that ****hsp70**** over-expression implies a potential role for these proteins in antigen processing and/or presentation resulting in an increased activity of APCs, which is essential for the initiation and modulation of the asthmatic ****immune**** ****response**** in chronic asthma. Fluticasone propionate induces downregulation of HLA-DR and ****hsp70**** molecules thus regulating inflammation by affecting key mechanisms of the allergic response.

21/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11080874 BIOSIS NO.: 199799702019
The mitochondrial hsp70 chaperone system. Effect of adenine nucleotides, peptide substrate, and mGrpE on the oligomeric state of mhsp70.

AUTHOR: Azem Abdussalam(a); Oppliger Wolfgang; Lustig Ariel; Jeno Paul; Feifel Bastian; Schatz Gottfried; Horst Martin
AUTHOR ADDRESS: (a)Biozentrum, Universitaet Basel, Klingelbergstrasse 70, CH-4056 Basel, Switzerland

JOURNAL: Journal of Biological Chemistry 272 (33):p20901-20906 1997
ISSN: 0021-9258
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Mitochondrial ****hsp70**** (mhsp70) is a key component in the import and folding of mitochondrial proteins. In both processes, mhsp70 cooperates with the mitochondrial nucleotide exchange factor mGrpE (also termed Mgelp). In this work we have characterized the self-association of purified mhsp70, the interaction of mhsp70 with isolated mGrpE and protein substrate, and the effect of nucleotides on these interactions. mhsp70 can form oligomers that are dissociated by ATP or by a ****nonhydrolyzable**** ATP analog. A substrate peptide binds to mhsp70 in the absence of added nucleotides and is released by ATP but not by ADP. Binding of the peptide causes nucleotide-independent dissociation of the mhsp70 oligomers and enhances the mhsp70 ATPase. Purified mGrpE forms a homodimer. In the absence of added nucleotides, one mGrpE dimer binds to one molecule of mhsp70, forming a stable 122 kDa hetero-oligomer. This ****complex**** is weakened by ADP and completely dissociated by ATP.

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L52          176 SEA FILE=WPIDS ABB=ON  HEAT SHOCK PROTEIN#
L58          494 SEA FILE=WPIDS ABB=ON  NON HYDROLY? OR NONHYDROLY?
L60            0 SEA FILE=WPIDS ABB=ON  L52 AND L58

=> dup rem l64,l63,l57
FILE 'MEDLINE' ENTERED AT 10:11:38 ON 06 JAN 1999

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FILE 'WPIDS' ENTERED AT 10:11:38 ON 06 JAN 1999
COPYRIGHT (C) 1999 DERWENT INFORMATION LTD
PROCESSING COMPLETED FOR L64
PROCESSING COMPLETED FOR L63
PROCESSING COMPLETED FOR L57
L65           32 DUP REM L64 L63 L57 (2 DUPLICATES REMOVED)

=> d bib ab l65 1-32; fil hom

L65  ANSWER 1 OF 32  CAPLUS  COPYRIGHT 1999 ACS        DUPLICATE 1
AN   1998:548556  CAPLUS
DN   129:156933
TI   Prevention and treatment of primary and metastatic neoplastic
     diseases and infectious diseases with heat shock
     /stress protein-peptide complexes
IN   Srivastava, Pramod K.; Chandawarkar, Rajiv Y.
PA   Fordham University, USA
SO   PCT Int. Appl., 90 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 9834641         A1   19980813      WO 98-US2193     19980203
         W:  AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE,
             GH, GW, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT,
             LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL,
             TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
     AU 9861455         A1   19980826      AU 98-61455      19980203
PRAI US 97-796319      19970207
     WO 98-US2193      19980203
AB   Methods and compns. are provided for eliciting an immune response
     and the prevention and treatment of primary and metastatic
     neoplastic diseases and infectious diseases.  The methods of the
     invention comprise administering a compn. comprising and effective
     amt. of a complex, in which the complex consists
     essentially of a heat shock protein (hsp)
     noncovalently bound to an antigenic mol.
     Optionally, the methods further comprise administering
     antigen-presenting cells sensitized with complexes of hsps
     noncovalently bound to an antigenic mol.  "
     Antigenic mol." as used herein refers to the peptides with
     which the hsps are endogenously assocd. in vivo as well as exogenous
     antigens/immunogens (i.e., with which the hsps are not
     complexed in vivo) or antigenic/immunogenic
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LANGUAGE: English

ABSTRACT: The interaction of the nucleotide-free molecular chaperone DnaK (****Hsp70****) from Escherichia coli with nucleotides was studied under equilibrium and transient kinetic conditions. These studies used the intrinsic fluorescence signal of the single tryptophan residue (Trp102) of DnaK, or of novel fluorescent nucleotide analogs of ADP and ATP, N-8-(4-N'-methylanthraniloylaminobutyl)-8-aminoadenosine 5'-di- or triphosphate (MABA-ADP and MABA-ATP) as spectroscopic probes. Titration of MABA-ADP with DnaK resulted in a 2.3-fold increase of the fluorescence signal, from which a binding stoichiometry of 1:1, and a dissociation constant (K-d) of 0.09 mu-M were derived. The intrinsic rate constant of hydrolysis of ATP or MABA-ATP in single turnover experiments was found to be 1.5 times 10-3 s-1 and 1.6 times 10-3 s-1, identical with the catalytic rate constant of 1.5(+- 0.17) times 10-3 s-1, obtained under steady-state conditions. The dissociation rate constant of ADP was measured to be 35(+- 7) times 10-3 s-1 in the absence or 15(+- 5) times 10-3 s-1 in the presence of 2 mM inorganic phosphate (P-i) and is therefore 10 to 20 times faster than the rate of hydrolysis. These results demonstrated that processes governing ATP hydrolysis are rate-limiting in the DnaK ATPase reaction cycle. The three observed different fluorescent states of the single tryptophan residue were investigated. The binding of ATP gave a decrease of 15% in fluorescence intensity compared with the nucleotide-free state. Subsequent ATP hydrolysis, or the simultaneous addition of ADP and P-i, increased the fluorescence 7% above the fluorescence intensity of the nucleotide-free protein. Changes in the tryptophan fluorescence could not be detected when ADP, Pi or the ****non****-****hydrolyzable**** nucleotide analogs AMPPNP (K-d = 1.62(+-0.1) mu-M) or ATP-gamma-S (K-d = 0.044(+-0.003) mu-M) were added. These data suggested that DnaK exists in at least three different conformational states, depending on nucleotide site occupancy. The fluorescence increase of DnaK upon ATP binding was resolved into two steps; a rapid first step (K-d1 = 7.3 mu-M) is followed by a second slow step (k+2 = 1.5 s-1 and k-2 ltoreq 1.5 times 10-3 s-1) that causes the decrease in the tryptophan fluorescence signal. The addition of ATP also resulted in the release of DnaK-****bound**** peptide substrate with k-off = 3.8 s-1, comparable with the rate of the second step of nucleotide binding. AMPPNP or ATP-gamma-S were not able to change the fluorescence signal nor to release the peptide. We therefore conclude that the second step of ATP binding, and not the 1000-fold slower ATP hydrolysis is coupled to peptide release.

21/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

10174559 BIOSIS NO.: 199698629477
The mitochondrial protein import machinery: Role of ATP in dissociation of the ****Hsp70**** cntdot Mim44 ****complex****.

AUTHOR: Von Ahsen Oliver; Voos Wolfgang; Henninger Hanspeter; Pfanner Nikolaus(a)
AUTHOR ADDRESS: (a)Biochemisches Inst., Univ. Freiburg, Hermann-Herder-Strasse 7, D-79104 Freiburg, Germany

JOURNAL: Journal of Biological Chemistry 270 (50):p29848-29853 1995
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

own blood - by subjecting it to oxidative stress, particularly for treating arthritis and scleroderma.

DC B04 D16
IN BOLTON, A E
PA (VASO-N) VASOGEN INC
CYC 75
PI WO 9807436 A1 980226 (9815)* EN 32 pp
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN YU ZW
AU 9738442 A 980306 (9830)
ADT WO 9807436 A1 WO 97-CA564 970811; AU 9738442 A AU 97-38442 970811
FDT AU 9738442 A Based on WO 9807436
PRAI US 96-754348 961122; GB 96-17611 960822
AB WO 9807436 A UPAB: 980410
Vaccine for alleviating symptoms of autoimmune disease comprises a sample of the patient's blood that has been modified so that, compared to an equal volume of normal blood, it has at least one of:

(a) more leucocytes showing increased intracellular vacuolation and abnormal smooth surface topography;

(b) fewer leucocytes expressing the major histocompatibility **complex** Class II molecule HLA-DR;

(c) up-regulated expression on leucocytes of the marker CD11-b;

(d) decreased levels of the **heat-shock proteins** (hsp) 60 and/or **70** in the lymphocytes;

(e) reduced ability of lymphocytes to proliferate in response to exogenous stimuli, and

(f) reduced ability of neutrophils to phagocytose and undergo the oxidative burst reaction.

USE - The vaccines are specifically used to treat (rheumatoid) arthritis and scleroderma, but more generally are useful in cases of graft vs. host disease, organ rejection, systemic lupus erythematosus, multiple sclerosis, psoriasis, endometriosis or allergy, inflammation. They may act by up-regulating Th2 cells and down-regulating Th1 cells.

The treated blood is administered at 0.01-400 (preferably 5-15) ml by intramuscular injection.

ADVANTAGE - Since the vaccines are based on the patient's own blood, they do not introduce any exogenous antigens.

Dwg.1/1

L65 ANSWER 4 OF 32 CAPLUS COPYRIGHT 1999 ACS
AN 1998:195155 CAPLUS
DN 128:202134
TI Isolation of processed, H-2Kb-binding ovalbumin-derived peptides associated with the stress proteins HSP70 and GP96
AU Breloer, Minka; Marti, Thomas; Fleischer, Bernhard; Von Bonin, Arne
CS Bernhard-Nocht Institute Tropical Medicine, Hamburg, D-20359, Germany
SO Eur. J. Immunol. (1998), 28(3), 1016-1021
CODEN: EJIMAF; ISSN: 0014-2980
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
AB Stress-induced proteins or **heat shock** proteins (HSP) of 96 kDa mass (**gp96**) and 70 kDa mass (HSP70) were shown previously to elicit specific immunity to tumors from which they are isolated. This immunity is dependent on CD8+ cytotoxic T cells which are readily primed in vivo by immunization with HSP.

chemical agents appear to target the p23 ****complex****, which is thought to enter at the last step in the assembly of the PR ****complex****. A model is presented to relate these findings to previous models and another ****complex**** between ****hsp90****, ****hsp70****, and p60 that appears to be an intermediate in PR assembly.

21/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09639998 BIOSIS NO.: 199598094916
Heat shock proteins in ****immune**** ****response**** to cancer: The Fourth Paradigm.

AUTHOR: Srivastava P K
AUTHOR ADDRESS: Dep. Biol. Sci., Fordham Univ., Bronx, NY 10458, USA

JOURNAL: Experientia (Basel) 50 (11-12):p1054-1060 1994
ISSN: 0014-4754
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The involvement of heat shock proteins in ****immune**** ****response**** is categorized into four distinct paradigms. In the First Paradigm, HSP derived from foreign organisms act as classical foreign antigens, and they elicit ****immune**** ****response**** to the non-conserved HSP epitopes. The Second Paradigm refers to instances where the host responds to self HSP to which there is no central or peripheral tolerance. The Third Paradigm involves molecular mimicry, where cross-reactivity between an HSP and another protein leads to an ****immune**** ****response**** to the latter under conditions which elicit an ****immune**** ****response**** to the former, such as infection with a bacterium whose immunodominant antigen is an HSP. The Fourth Paradigm refers to situations where an HSP-antigen ****complex**** elicits an effective response to the antigen and not to the HSP. Thus the HSP acts as a carrier for the ****antigenic**** peptide. The role of HSP in recognition by gamma-delta T cells may also fall into this paradigm. In this article, the Fourth Paradigm is considered as a crucial element in the development of vaccines against cancers and infectious diseases, and is analyzed through the prism of the observed association of ****hsp70**** species with ****antigenic**** peptides.

21/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09538673 BIOSIS NO.: 199497547043
Mitochondrial GrpE is present in a ****complex**** with ****hsp70**** and preproteins in transit across membranes.

AUTHOR: Voos Wolfgang; Gambill B Diane; Laloraya Shikha; Ang Deborah; Craig Elizabeth A; Pfanner Nikolaus(a)
AUTHOR ADDRESS: (a)Biochemisches Inst., University Freiburg, Hermann-Herder-Strasse 7, D-79104 Freiburg, Germany

JOURNAL: Molecular and Cellular Biology 14 (10):p6627-6634 1994
ISSN: 0270-7306
DOCUMENT TYPE: Article
RECORD TYPE: Abstract

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9710001	A1	19970320	WO 96-US14557	19960911
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, FI, GE, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5837251	A	19981117	US 95-527391	19950913
	AU 9670181	A1	19970401	AU 96-70181	19960911
	EP 859631	A1	19980826	EP 96-931527	19960911
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 95-527391	19950913			
	WO 96-US14557	19960911			

AB Methods and compns. are disclosed for eliciting an immune response and the prevention and treatment of primary and metastatic neoplastic diseases and infectious diseases. The methods comprise administering a compn. comprising an effective amt. of a **complex**, in which the **complex** consists essentially of a **heat shock** protein (hsp) noncovalently **bound** to an **antigenic** mol. "**Antigenic** mol." refers to the peptides with which the hsps are endogenously assocd. in vivo as well as exogenous antigens/immunogens (i.e., with which the hsps are not **complexed** in vivo or **antigenic**/immunogenic fragments and derivs. thereof). In a preferred embodiment, the **complex** is autologous to the individual. The effective amts. of the **complex** are in the range of 100-600 .mu.g for **complexes** comprising hsp70, 50-1000 .mu.g for hsp90, and 10-600 .mu.g for **gp96**. The invention also provides a method for measuring tumor rejection in vivo in an individual, preferably a human, comprising a measuring the generation by the individual of MHC Class I-restricted CD8+ cytotoxic T-lymphocytes specific to the tumor. Methods of purifying hsp70-peptide **complexes** are also provided. Administration of **gp96** prepns. derived from UV-induced carcinomas immunized syngeneic mice from the resp. cancer cell type.

L65 ANSWER 7 OF 32 CAPLUS COPYRIGHT 1999 ACS
AN 1997:257526 CAPLUS
DN 126:233700
TI Immunotherapy of cancer and infectious disease using antigen-presenting cells sensitized with **heat-shock** protein-antigen **complexes**
IN Srivastava, Pramod K.
PA Fordham University, USA
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9710002	A1	19970320	WO 96-US14558	19960911
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, FI, GE, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

hsc70 during heat stress, which may explain, at least in part, why ****hsp70**** proteins accumulate in the nucleus, particularly the nucleolus. This interaction may limit heat-induced protein damage and/or accelerate restoration of protein function in an ATP-independent reaction.

21/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

08311598 BIOSIS NO.: 000094073921
AN 80-KILODALTON ANTIGEN FROM HISTOPLASMA-CAPSULATUM THAT HAS HOMOLOGY TO HEAT SHOCK PROTEIN 70 INDUCES CELL-MEDIATED ****IMMUNE**** ****RESPONSES**** AND PROTECTION IN MICE

AUTHOR: GOMEZ F J; GOMEZ A M; DEEPE G S JR
AUTHOR ADDRESS: DIV. INFECT. DIS., DEP. INTERNAL MED., UNIV. CINCINNATI COLL. MED., CINCINNATI, OHIO 45267-0560.

JOURNAL: INFECT IMMUN 60 (7). 1992. 2565-2571.
FULL JOURNAL NAME: Infection and Immunity
CODEN: INFIB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: An extract of the cell wall and cell membrane from Histoplasma capsulatum yeast cells was assayed by Western blot (immunoblot) for reactivity with two monoclonal antibodies to ****heat**** ****shock**** ****protein**** ****70****. Four bands with molecular masses of 80, 66, 54, and 32 kDa ****bound**** both antibodies. The 80-kDa protein was isolated, analyzed for homology to ****heat**** ****shock**** ****protein**** ****70****, and tested for ****antigenicity**** and immunogenicity in C57BL/6 mice. The 80-kDa protein reacted with monoclonal antibody to ****heat**** ****shock**** ****protein**** ****70****. Sera from mice immunized with the antigen recognized H. capsulatum ****heat**** ****shock**** ****protein**** ****70****. Moreover, the amino-terminal sequence of the 80-kDa protein revealed substantial homology with ****heat**** ****shock**** ****protein**** ****70**** from several species. The 80-kDa protein induced delayed-type hypersensitivity responses in mice immunized with either viable yeast cells or antigen. Splenocytes from mice immunized with yeast cells or with antigen responded in vitro to the 80-kDa antigen. Immunization of mice with the antigen enhanced host resistance against a sublethal inoculum of H. capsulatum yeast cells, but it did not reduce the mortality of mice given a lethal challenge of yeast cells. Thus, this antigen manifests homology with members of the ****heat**** ****shock**** ****protein**** ****70**** family. Furthermore, the 80-kDa protein elicits cellular ****immune**** ****responses**** to H. capsulatum, and it mediates protective immunity.

21/7/11 (Item 11 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

08311046 BIOSIS NO.: 000094073369
THE HUMAN HEAT SHOCK PROTEIN HSP70 INTERACTS WITH HSF THE TRANSCRIPTION FACTOR THAT REGULATES HEAT SHOCK GENE EXPRESSION

AUTHOR: ABRAVAYA K; MYERS M P; MURPHY S P; MORIMOTO R I
AUTHOR ADDRESS: DEP. BIOCHEMISRY, MOLECULAR BIOLOGY CELL BIOLOGY,

L65 ANSWER 9 OF 32 MEDLINE
AN 1998040279 MEDLINE
DN 98040279
TI Interactions between cationic liposomes and an antigenic protein: the physical chemistry of the immunoadjuvant action.
AU Tsuruta L R; Quintilio W; Costa M H; Carmona-Ribeiro A M
CS Departamento de Bioquimica, Instituto de Quimica, S. Paulo, SP, Brazil.
SO JOURNAL OF LIPID RESEARCH, (1997 Oct) 38 (10) 2003-11.
Journal code: IX3. ISSN: 0022-2275.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199803
EW 19980304
AB The 18 kDa antigenic protein from Mycobacterium leprae (P) or its N-acyl derivative (AP) was incorporated in dioctadecyldimethylammonium bromide (DODAB) liposomes in water or in phosphate-buffered saline (PBS). In water, 100% P incorporation in liposomes contrasts with 65% in PBS. There is 75-80% AP incorporation to liposomes in water against 55-65% in PBS, showing that attachment of hydrophobic residues to the protein, instead of increasing, further decreases incorporation to the liposomes. From protein adsorption on latex, P affinity is larger than AP affinity for the latex surface whereas limiting adsorption for AP is much larger than that obtained for P, possibly due to AP aggregation in solution. P-induced rupture of liposomes containing [14C]sucrose was evaluated from dialysis of protein/liposomes mixtures. In water, P incorporation to the liposomes causes leakage of radioactive contents contrasting with the absence of leakage for P incorporation in PBS. Immunization tests for delayed type hypersensitivity indicate a enhancement of cell-mediated immunological response towards P/DODAB **complexes** that is not obtained for the isolated protein. Absence of leakage for P in PBS is associated with a P "lying-over" on the liposome and optimization of protein presentation to the immunological system.

L65 ANSWER 10 OF 32 MEDLINE
AN 97458239 MEDLINE
DN 97458239
TI Immunotherapy of tumors with autologous tumor-derived heat shock protein preparations.
AU Tamura Y; Peng P; Liu K; Daou M; Srivastava P K
CS Center for Immunotherapy of Cancer and Infectious Diseases, MC1601, University of Connecticut School of Medicine, Farmington, CT 06030, USA.
NC CA44786 (NCI)
CA64394 (NCI)
SO SCIENCE, (1997 Oct 3) 278 (5335) 117-20.
Journal code: UJ7. ISSN: 0036-8075.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199712
EW 19971204
AB Immunotherapy of mice with preexisting cancers with heat shock protein preparations derived from autologous cancer resulted in retarded progression of the primary cancer, a reduced metastatic load, and prolongation of life-span. Treatment with heat shock

binding of GrpE required DnaK. Inactivation of DnaJ, GrpE, and GroES did not affect the association or dissociation of DnaK or GroEL from CRAG. The DnaK and GrpE proteins could be eluted with 10-6 M ATP, but 10-4 M was required for GroEL release. This approach allows a one-step purification of these proteins from E. coli and also the isolation of the DnaK and GroEL homologs from yeast mitochondria. Competition experiments with oligopeptide fragments of CRAG showed that DnaK and GroEL interact with different sites on CRAG and that the cro-derived domain of CRAG contains the DnaK-binding site.

21/7/13 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

10747255 EMBASE No: 98173954

Heat shock protein 70 upregulation is related to HLA-DR expression in bronchial asthma. Effects of inhaled glucocorticoids

Bertorelli G.; Bocchino V.; Zhuo X.; Chetta A.; Del Donno M.; Foresi A.; Testi R.; Olivieri D.

Dr. G. Bertorelli, Department of Respiratory Disease, University of Parma, Rasori Hospital, Via Rasori 10, 43100 Parma Italy

Clinical and Experimental Allergy (United Kingdom) , 1998, 28/5 (551-560)
CODEN: CLEAE ISSN: 0954-7894
DOCUMENT TYPE: Journal ; Article
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH
NUMBER OF REFERENCES: 53

Background and objective: Antigen processing determines the production of peptides from antigens - including allergens - and their binding to class II major histocompatibility complex molecules, that stimulate T-cell responses. Heat shock protein (****hsp****) ****70**** are recognized to have a role in chaperoning ****antigenic**** peptides and in facilitating class II peptide assembly. We studied the HLA-DR and ****hsp70**** expression on BAL cells and bronchial biopsies from asthmatics, as well as the effect of low dose fluticasone propionate treatment. Methods: Twenty-three asthmatics and eight normal subjects were selected. In each subject BAL and bronchial biopsies were performed. Eighteen out of 23 asthmatics, underwent the second bronchoscopy after 6 weeks of low dose inhaled fluticasone propionate treatment (250 microg bd) in a placebo-controlled double-blind study. BAL fluid and biopsies were processed to evaluate HLA-DR and ****hsp70**** expression by immunochemistry methods. Results: ****Hsp70**** and HLA-DR upregulation was present on professional and non- professional antigen presenting cells (APCs). In asthmatics, the ****hsp70**** and HLA-DR expression was higher in BAL (****hsp70**** $P < 0.001$, HLA-DR $P < 0.001$) and bronchial epithelium (****hsp70**** $P < 0.001$, HLA-DR $P < 0.001$) when compared with controls. We also observed a significant correlation between ****hsp70**** and HLA- DR expression in BAL ($P < 0.005$) and epithelium ($P < 0.001$). Fluticasone propionate treatment down-regulated the ****hsp70**** and HLA-DR expression in BAL (****hsp70**** $P < 0.001$, HLA-DR $P < 0.05$) and bronchial epithelium (****hsp70**** $P < 0.05$, HLA-DR $P < 0.05$). A serial section comparison study showed that CD1a+ cells and macrophages were positive for both ****hsp70**** and HLA-DR in the submucosa. Conclusions: Our results support the hypothesis that ****hsp70**** over-expression implies a potential role for these proteins in antigen processing and/or presentation resulting in an increased activity of APCs, which is essential for the initiation and modulation of the asthmatic ****immune**** ****response**** in chronic asthma. Fluticasone propionate induces down-regulation of HLA-DR and ****hsp70**** molecules thus regulating inflammation by affecting key mechanisms of the allergic response.

Journal code: IFE. ISSN: 0022-1759.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199709
EW 19970904
AB Adenosine triphosphate (ATP)-affinity chromatography has been widely used to purify molecules of the Hsp70 family. This procedure leads to dissociation of peptides from Hsp70 molecules, resulting in Hsp70 preparations devoid of immunological activity. We report that substitution of ATP-affinity chromatography by ADP-affinity chromatography results in isolation of Hsp70 molecules which are still associated with peptides and are immunogenic. The Hsp70 preparations thus obtained contain the constitutive Hsp73 and the inducible Hsp72 molecules. These observations furnish a basis for an analysis of the structural heterogeneity among the members of the Hsp70 family and of the antigenic peptides associated with individual members of this family. They also provide a practical method for the isolation of large quantities of immunologically active Hsp70-peptide preparations.

L65 ANSWER 13 OF 32 CAPLUS COPYRIGHT 1999 ACS
AN 1996:367135 CAPLUS
DN 125:52050
TI Purification and characterization of the **heat shock** proteins HslV and HslU that form a new ATP-dependent protease in Escherichia coli
AU Yoo, Soon Ji; Seol, Jae Hong; Shin, Dong Hun; Rohrwild, Markus; Kang, Man-Sik; Tanaka, Keiji; Goldberg, Alfred L.; Chung, Chin Ha
CS Coll. Nat. Sci., Seoul Natl. Univ., Seoul, 151-742, S. Korea
SO J. Biol. Chem. (1996), 271(24), 14035-14040
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB The hslVU operon in Escherichia coli encodes two **heat shock** proteins, HslV, a 19-kDa protein homologous to .beta.-type subunits of the 20S proteasomes, and HslU, a 50-kDa protein related to the ATPase ClpX. The authors have recently shown that HslV and HslU can function together as a novel ATP-dependent protease, the HslVU protease. The authors have now purified both proteins to apparent homogeneity from exts. of E. coli carrying the hslVU operon on a multi-copy plasmid. HslU by itself cleaved ATP, and pure HslV is a weak peptidase degrading certain hydrophobic peptides. HslU dramatically stimulated peptide hydrolysis by HslV when ATP is present. With a 1:4 molar ratio of HslV to HslU, approx. a 200-fold increase in peptide hydrolysis was obsd. HslV stimulated the ATPase activity of HslU 2-4-fold, but had little influence on the affinity of HslU to ATP. The **nonhydrolyzable** ATP analog .beta.,.gamma.-methylene-ATP did not support peptide hydrolysis. Other nucleotides (CTP, dATP) that were slowly hydrolyzed by HslU allowed some peptide hydrolysis. Therefore, ATP cleavage appears essential for the HslV activity. Upon gel filtration on a Sephacryl S-300 **column**, HslV behaved as a 250-kDa oligomer (i.e. 12-14 subunits), and HslU behaved as a 100-kDa protein (i.d. a dimer) in the absence of ATP, but as a 450-kDa multimer (8-10 subunits) in its presence. Therefore ATP appears necessary for oligomerization of HslU. Thus the HslVU protease appears to be a two-component protease in which HslV harbors the peptidase activity, while HslU provides an essential ATPase activity.

21/7/16 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

7873094 EMBASE No: 90308178
Microbial stress proteins
Watson K.
Department of Biochemistry, Microbiology and Nutrition, University of New England, Armidale, NSW 2351 Australia
ADV. MICROB. PHYSIOL. (United Kingdom) , 1990, 31/- (183-223)
CODEN: AMIPB
LANGUAGES: English

There is general agreement that a function, perhaps the major function, of stress proteins under normal physiological conditions is to help assembly and disassembly of protein ****complexes**** and to catalyse protein-translocation processes. It remains unclear, however, as to what role these processes play in stressed cells. It could be that cells under stress produce abnormal, misfolded or otherwise damaged proteins and that increased synthesis of stress proteins is required to counter protein modifications. A role for stress proteins in recovery of cells from stress, as opposed to a role in helping cells to withstand a lethal stress, is thus suggested. The intracellular location of stress proteins, in the unstressed and stressed cell, is worthy of further studies. Members of the ****hsp70**** family are associated with the cytosol, mitochondria and endoplasmic reticulum. There is evidence, particularly from studies on mammalian cells (Tanguay, 1985; Welch and Mizzen, 1988; Arrigo et al., 1988), that following stress hsps migrate to various cellular compartments and subsequently delocalize after stress. However, there is little comparable data from microbial systems for this phenomenon (e.g. Rossi and Lindquist, 1989). The question as to the role of stress proteins in the transient acquisition of thermotolerance remains to be answered. It is insufficient to equate the kinetics of stress-protein synthesis with acquisition of thermotolerance. Quantitative data on the amount of stress protein present at various times, including the recovery period, is required. The demonstration that microbial stress proteins are important ****antigenic**** determinants of micro-organisms causing major debilitating diseases in the world is an exciting observation. Studies on the interplay of pathogen and host, both carrying similar ****antigenic**** hsp determinants, will be a challenging area for future research. It is likely that E. coli and Sacch. cerevisiae, with their well-established biochemical and genetic properties, will continue to be the experimental systems of choice for studies on stress proteins. On the other hand, it is encouraging that studies on other micro-organisms have expanded in the past few years and have made substantial contributions towards our understanding of the stress response. The ubiquitous nature of the stress response and the remarkable evolutionary conservation of the stress proteins continue to the attractive areas for research.

AN 95-283728 [37] WPIDS
DNN N95-215931 DNC C95-128032
TI Detecting wheat exposed to high temp. during grain filling - by determining level of **heat shock protein** in the endosperm; used to assess suitability of grain for baking.
DC C07 D11 S03
IN BERNARDIN, J E
PA (USDA) US SEC OF AGRIC
CYC 20
PI WO 9521190 A1 950810 (9537)* EN 34 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA MX
AU 9517393 A 950821 (9547)
US 5789180 A 980804 (9838)
ADT WO 9521190 A1 WO 95-US1324 950201; AU 9517393 A AU 95-17393 950201; US 5789180 A Cont of US 94-192873 940207, US 95-543233 951013
FDT AU 9517393 A Based on WO 9521190
PRAI US 94-192873 940207; US 95-543233 951013
AB WO 9521190 A UPAB: 950921
Wheat grain that has been exposed to high temp. during the grain filling process is detected by: (1) extracting a wheat heat stress peptide (I) from an endosperm-contg. sample of the grain; (2) measuring the level of (I) in the sample and (3) comparing this with the constitutive level (CL); if the measured level is 2 CL this indicates exposure to high temp. (I) is reactive with antibodies (Ab) to an epitope equiv. to that between amino acids 504-617 of human hsp **70**. Also claimed are: (1) isolated (I) reactive with Ab and present at above CL (even after protein synthesis in the grain has ceased) if the grain has been exposed to high temp.; and (2) a kit (esp. a dipstick) for detecting (I) comprising: (i) a reagent that selectively binds (I); (ii) an immunological binding partner that binds to **bound** (I); and (iii) reagent for detecting this binding partner.
USE - The method is used to determine if wheat is suitable for a particular application, e.g. to assess is dough properties, mixing or baking performance. Measurement of (I) gives an indication of integrated heat exposure.
ADVANTAGE - Elevated (I) levels are maintained even in the dormant state (most heat stress responses are transient). The method is sensitive, rapid, selective, inexpensive and simple enough for use in the field.
Dwg.0/6

L65 ANSWER 17 OF 32 MEDLINE
AN 96102038 MEDLINE
DN 96102038
TI The mitochondrial protein import machinery. Role of ATP in dissociation of the Hsp70.Mim44 complex.
AU von Ahsen O; Voos W; Henninger H; Pfanner N
CS Biochemisches Institut, Universitat Freiburg, Federal Republic of Germany.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Dec 15) 270 (50) 29848-53. Journal code: HIV. ISSN: 0021-9258.
wrong date
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199604
AB Interaction of preproteins with the heat shock protein Hsp70 in the mitochondrial matrix is required for driving protein transport across the mitochondrial inner membrane. Binding of mt-Hsp70 to the protein Mim44 of the inner membrane import site seems to be an

essential part of an ATP-dependent reaction cycle. However, the available results on the role played by ATP are controversial. Here we demonstrate that the mt-Hsp70.Mim44 complex contains ADP and that a **nonhydrolyzable** analog of ATP dissociates the mt-Hsp70.Mim44 complex in the presence of potassium ions. The previously reported requirement of ATP hydrolysis for complex dissociation was due to the use of a nonphysiological concentration of sodium ions. In the presence of potassium ions, mt-Hsp70 undergoes a conformational change that is not observed with a mutant Hsp70 defective in binding to Mim44. The mutant Hsp70 is able to bind substrate proteins, differentiating binding to Mim44 from binding to substrate proteins. We conclude that binding of ATP, not hydrolysis, is required to dissociate the mt-Hsp70.Mim44 complex and that the reaction cycle includes an ATP-induced conformational change of mt-Hsp70.

L65 ANSWER 18 OF 32 MEDLINE
AN 95327619 MEDLINE
DN 95327619
TI The DnaJ chaperone catalytically activates the DnaK chaperone to preferentially bind the sigma 32 heat shock transcriptional regulator.
AU Liberek K; Wall D; Georgopoulos C
CS Department of Molecular Biology, University of Gdansk, Poland.
NC GM38346 (NIGMS)
CA46128 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Jul 3) 92 (14) 6224-8.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199510
AB In Escherichia coli the heat shock response is under the positive control of the sigma 32 transcription factor. Three of the heat shock proteins, DnaK, DnaI, and GrpE, play a central role in the negative autoregulation of this response at the transcriptional level. Recently, we have shown that the DnaK and DnaJ proteins can compete with RNA polymerase for binding to the sigma 32 transcription factor in the presence of ATP, by forming a stable DnaJ-sigma 32-DnaK protein complex. Here, we report that DnaJ protein can catalytically activate DnaK's ATPase activity. In addition, DnaJ can activate DnaK to bind to sigma 32 in an ATP-dependent reaction, forming a stable sigma 32-DnaK complex. Results obtained with two DnaJ mutants, a missense and a truncated version, suggest that the N-terminal portion of DnaJ, which is conserved in all family members, is essential for this activation reaction. The activated form of DnaK binds preferentially to sigma 32 versus the bacteriophage lambda P protein substrate.

L65 ANSWER 19 OF 32 MEDLINE
AN 96062035 MEDLINE
DN 96062035
TI Induction of diabetes in standard mice by immunization with the p277 peptide of a 60-kDa heat shock protein.
AU Elias D; Marcus H; Reshef T; Ablamunits V; Cohen I R
CS Department of Cell Biology, Weizmann Institute of Science, Rehovot, Israel.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1995 Oct) 25 (10) 2851-7.
Journal code: EN5. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199602
AB We previously reported that immunity to the p277 peptide of the human 60-kDa heat shock protein (hsp60) was a causal factor in the diabetes of non-obese diabetic (NOD) mice, which are genetically prone to develop spontaneous autoimmune diabetes. The present study was done to test whether immunization with the p277 peptide could cause diabetes in standard strains of mice. We now report that a single administration of the p277 peptide conjugated to carrier molecules such as bovine serum albumin or ovalbumin can induce diabetes in C57BL/6 mice and in other strains not genetically prone to develop diabetes. The diabetes was marked by hyperglycemia, insulitis, insulin autoantibodies, glucose intolerance and low blood levels of insulin. The diabetes could be transferred to naive recipients by anti-p277 T cell lines. Similar to other experimentally induced autoimmune diseases, the autoimmune diabetes remitted spontaneously. After recovery, the mice were found to have acquired resistance to a second induction of diabetes. Susceptibility to induced diabetes in C57BL/6 mice was influenced by sex (males were much more susceptible than were females) and by class II genes in the major histocompatibility **complex** (B6.H-2bm12 mice with a mutation in the MHC-II molecule were relatively resistant). Other strains of mice susceptible to induced diabetes were C57BL/KSJ, C3HeB/FeJ, and NON/Lt. BALB/c and C3H/HeJ strains were relatively resistant. Immunization to p277-carrier conjugates could also induce transient hyperglycemia in young NOD mice, but upon recovery from the induced diabetes, the NOD mice were found to have acquired resistance to later development of spontaneous diabetes. Thus, T cell immunity to the p277 peptide can suffice to induce diabetes in standard mice, and a short bout of induced diabetes can affect the chronic process that would otherwise lead to spontaneous diabetes in diabetes-prone NOD mice.

L65 ANSWER 20 OF 32 MEDLINE
AN 95335744 MEDLINE
DN 95335744
TI Decrease in heart peptide initiation during head-down tilt may be modulated by HSP-70.
AU Menon V; Yang J; Ku Z; Thomason D B
CS Department of Physiology and Biophysics, University of Tennessee Health Science Center, Memphis 38163, USA..
NC AR-40901 (NIAMS)
SO AMERICAN JOURNAL OF PHYSIOLOGY, (1995 Jun) 268 (6 Pt 1) C1375-80. Journal code: 3U8. ISSN: 0002-9513.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199510
AB This study examines the mechanism of the rapid decrease in cardiac muscle protein synthesis during rodent hindlimb non-weight bearing. Polysomes isolated from rat hearts 8 h after suspension show less RNA in the polysome pool and a shift in polysome size toward fewer ribosomes per mRNA; 18 h after suspension, the size shift persists, but the amount of RNA in the polysome pool returns to control values. These data are consistent with a decrease in the rate of initiation of protein synthesis. At both 8 and 12 h of suspension, the cardiac polysomes show a 78 and 93% increase association with the nascent polypeptide chaperone protein 70-kDa heat-shock cognate/heat-shock protein (HSC/HSP-70), respectively, that persists

after 7 days of non-weight bearing. Because the dissociation of HSC/HSP-70 from unfolded protein can be modulated by ATP, we measured the adenosine nucleotide pools and found a 53% decrease in ATP levels after 18 h of suspension. We propose a mechanism in which a shift of HSC/HSP-70 to the nascent polypeptide indirectly inhibits protein synthesis initiation.

L65 ANSWER 21 OF 32 MEDLINE
AN 1998299913 MEDLINE
DN 98299913
TI Human stress protein hsp70: overexpression in E coli, purification and characterization.
AU Jindal S; Murray P; Rosenberg S; Young R A; Williams K P
CS PerSeptive Biosystems, Framingham, MA, USA.
SO BIO/TECHNOLOGY, (1995 Oct) 13 (10) 1105-9.
Journal code: AL1. ISSN: 0733-222X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; B
EM 199809
EW 19980904
AB The gene encoding the stress-inducible member of human heat shock protein hsp70, was expressed in E. coli using the bacteriophage T7 RNA polymerase-based gene expression system. Recombinant hsp70 (R-hsp70) was purified from inclusion bodies after solubilization and refolding, using a combination of ATP-agarose affinity chromatography and ion-exchange chromatography. R-hsp70 was shown to be monomeric and free of its structurally similar E. coli counterpart, DnaK. In addition, R-hsp70 is functional as demonstrated by its ability to bind to peptides and to ATP. The availability of pure, correctly folded R-hsp70 in sufficient quantity will assist in the structural and functional characterization of hsp70. Furthermore, an understanding of the cytoprotective function of hsp70 and its role in immune responses during infections will be facilitated by the availability of pure R-hsp70.

L65 ANSWER 22 OF 32 MEDLINE
AN 95235961 MEDLINE
DN 95235961
TI Purification and characterization of HSP70 proteins from Torpedo electric organ.
AU Eichler J; Tolliday N; Toker L; Silman I
CS Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel..
SO Comp Biochem Physiol B Biochem Mol Biol, (1995 Feb) 110 (2) 409-15.
Journal code: CF9.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199507

L65 ANSWER 23 OF 32 MEDLINE
AN 95322860 MEDLINE
DN 95322860
TI Spinach leaf 70-kilodalton heat-shock cognate stabilizes bovine adrenal glucose-6-phosphate dehydrogenase in vitro without apparent stable binding.
AU Anderson J V; Guy C L
CS Department of Environmental Horticulture, University of Florida,

Gainesville 32611-0512, USA..
SO PLANTA, (1995) 196 (2) 303-10.
Journal code: BNG. ISSN: 0032-0935.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; B
EM 199510
AB Spinach (Spinacia oleracea L.) leaf tissue 70-kilodalton heat-shock cognate was purified by ATP-agarose affinity and gel filtration. Gel filtration of the affinity-purified protein resolved it into three forms: monomer, dimer, and oligomer. In the absence of ATP, the majority of the heat-shock cognate existed as a monomeric form with lesser amounts of dimer and oligomer. Addition of 3 mM ATP to the purified protein, containing all three forms, converted the dimeric and monomeric forms to a high-molecular-weight complex. Removal of ATP from the complex by dialysis resulted in the reappearance of the dimeric and monomeric forms. Addition of ATP to the highly purified monomer had no effect on its gel-filtration migration. Neither purified monomeric or dimeric forms showed stable binding to denatured proteins; however, both forms of the purified heat-shock cognate were able to stabilize the enzymatic activity of bovine adrenal glucose-6-phosphate dehydrogenase over a 48-h period at 25 degrees C. In addition, the activity of glucose-6-phosphate dehydrogenase in the presence of purified heat-shock cognate dimer or monomer could be rapidly decreased in an ATP-dependent fashion depending on the order of the substrate addition to the reaction mixture. Circular-dichroism studies indicated that addition of ATP to the spinach 70-kDa heat-shock cognate caused a conformation change from alpha-helical to a greater beta-sheet content. How conformational character may influence the stabilizing activity of the heat-shock cognate in a mechanism which does not require stable peptide binding is discussed.

L65 ANSWER 24 OF 32 MEDLINE
AN 95127110 MEDLINE
DN 95127110
TI Heat shock protein-peptide **complexes** in cancer immunotherapy.
AU Srivastava P K; Udono H
CS Department of Biological Sciences, Fordham University, Bronx, New York 10458..
SO CURRENT OPINION IN IMMUNOLOGY, (1994 Oct) 6 (5) 728-32. Ref: 30
Journal code: AH1. ISSN: 0952-7915.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199504
AB Heat shock proteins (HSPs) are associated with a broad spectrum of peptides derived from the cells from which they are isolated. Vaccination with such HSP-peptide **complexes** elicits protective immunity against tumors or other cells used as the source of HSPs. These observations suggest that HSP-peptide **complexes** are suitable as vaccines against cancers and infectious diseases.

L65 ANSWER 25 OF 32 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 93-351876 [44] WPIDS
DNN N93-271381 DNC C93-156243
Searched by Barb O'Bryen, STIC 308-4291

TI Identifying tumour cells which induce p53 auto-antibodies - by formation of mutant p53 **complex** with **heat shock protein**, for diagnosis, prognosis and monitoring of tumours.
DC B04 S03
IN DAVIDOFF, A M; HENSLEE, J G; IGLEHART, J D; MARKS, J R; INGLEHART, J D
PA (ABBO) ABBOTT LAB; (UYDU-N) UNIV DUKE; (SUMO) SUMITOMO CHEM CO LTD
CYC 22
PI WO 9321529 A1 931028 (9344)* EN 47 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: AU CA JP KR
AU 9340245 A 931118 (9410)
EP 636248 A1 950201 (9509) EN
R: BE CH DE ES FR GB IT LI
JP 07505719 W 950622 (9533) 13 pp
EP 636248 A4 961113 (9712)
US 5652115 A 970729 (9736) 15 pp
ADT WO 9321529 A1 WO 93-US2831 930326; AU 9340245 A AU 93-40245 930326; EP 636248 A1 EP 93-909458 930326, WO 93-US2831 930326; JP 07505719 W JP 93-518355 930326, WO 93-US2831 930326; EP 636248 A4 EP 93-909458 ; US 5652115 A CIP of US 92-869292 920414, Cont of US 92-968818 921030, US 94-276872 940718
FDT AU 9340245 A Based on WO 9321529; EP 636248 A1 Based on WO 9321529; JP 07505719 W Based on WO 9321529
PRAI US 92-968818 921030; US 92-869292 920414; US 94-276872 940718
AB WO 9321529 A UPAB: 971222
Tumour cells are classified according to their ability to produce serum p53 (tumour suppressor gene) autoantibodies (Ab) in a patient by detecting, in a tumour cell sample, the presence of a **complex** (A) between p53 protein and a 70kD **heat-shock protein** (hsp70). If (A) is detected the cells are able to elicit Ab prodn.

Also new are (1) diagnosis of tumours (including recurrence in treated patients) by detecting Ab, indicating that tumour cells produce a mutant p53 able to form a **complex** with hsp70; the presence of Ab also indicates tumour cells of high tumorigenic potential able to combat more aggressive disease; and (2) immunoassays for quantification of Ab.

Pref. the tumour cells are of epithelial origin, partic. colorectal, lung, breast (esp.) or ovarian cancer cells.

USE/ADVANTAGE - p53 mutants able to **complex** with hsp70 are able to induce Ab and are associated with more aggressive cancers. Detection of Ab can thus be used for prognosis, diagnosis and monitoring of cancer (including formation of metastases after removal of the prim. tumour).
Dwg.0/5

L65 ANSWER 26 OF 32 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 93-303460 [38] WPIDS
DNC C93-135206
TI New protein forming **complex** with **heat shock protein** - also binding immuno-suppressors, etc., and corresp. nucleic acid antibodies etc., useful e.g. for detecting tumours, treating auto-immune disease, etc..
DC B04 D16
IN BAULIEU, E; CALLEBAUT, I; CHAMBRAUD, B; LEBEAU, M; MASSOL, N; MORNON, J; RADANYI, C; RENOIR, M
PA (INRM) INSERM INST NAT SANTE & RECH MEDICALE
CYC 18
PI WO 9318146 A2 930916 (9338)* FR 43 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

W: JP US
FR 2688227 A1 930910 (9346) 37 pp
WO 9318146 A3 931111 (9514)
ADT WO 9318146 A2 WO 93-FR219 930304; FR 2688227 A1 FR 92-2612 920304; WO 9318146 A3 WO 93-FR219 930304
PRAI FR 92-2612 920304
AB WO 9318146 A UPAB: 931123
New nucleotide sequence (I) comprises, or consists of, a chain which can hybridise under stringent conditions, with one or more sequences of a gene the cDNA from which has a structure defined in the specification.

Also new are (1) RNA (and complementary sequences) and proteins derived from (I); (2) recombinant cloning and expression vectors contg. (I); (3) microorganisms contg. (I) or these vectors; (4) amino acid sequences (A) deduced from (I); (5) **complexes** of (A) with **heat shock protein** (hsp) **90**, or other hsp; (6) antibodies (monoclonal or polyclonal) specific for (A) and their **complexes**.

Partic. (I) contains all or part of the open reading frame extending from position 4 to 1380 of the specified sequence.

USE/ADVANTAGE - (I), isolated from rabbit liver, encodes a protein able to **complex** hsp **90** (a 'chaperone' protein which can bind to many ligands such as steroid hormone receptors, vitamin D, and tyrosine kinases of viral oncogenes), even when this is part of a hetero-oligomer with other proteins. (I)-derived probes can be used to detect genes producing protein reactive with hsp 60, esp. early expression of such genes may be useful for assessing development and/or differentiation of tumours. Antibodies can be used to detect expression products of (I), also to detect immunosuppressor receptors and to reduce the endocrinal side effects of immunosuppressors. (A) can be used to study, prevent or treat diseases (e.g. autoimmune disease, cancer, rickets, or dioxin poisoning) associated with dysfunction of proteins which form **complexes** with hsp90 and to localise such proteins. In particular, the proteins reactive with hsp **90** are normally confined to the nucleus but in tumour cells are also present in the cytoplasm.
Dwg.0/8

L65 ANSWER 27 OF 32 CAPLUS COPYRIGHT 1999 ACS
AN 1993:537033 CAPLUS
DN 119:137033
TI Tumor rejection antigen gp96/grp94 is an ATPase: implications for protein folding and antigen presentation
AU Li, Zihai; Srivastava, Pramod K.
CS Dep. Pharmacol., Mount Sinai Sch. Med., New York, NY, 10029, USA
SO EMBO J. (1993), 12(8), 3143-51
CODEN: EMJODG; ISSN: 0261-4189
DT Journal
LA English
AB Immunization of mice with **gp96/grp94 heat shock** proteins (HSPs) elicits tumor-specific cellular immunity to the tumors from which **gp96** is isolated. However, the cDNA sequence of **gp96** is identical among tumors and normal tissues. This raises the question regarding the structural basis of the specific immunogenicity of **gp96**. As HSPs bind a wide array of mols. including peptides, the authors have proposed that **gp96** may not be immunogenic per se, but may chaperone **antigenic** peptides. Furthermore, **gp96** is localized predominantly in the lumen of the endoplasmic reticulum (ER) suggesting that it may act as a peptide acceptor and as accessory to peptide loading of MHC class I mols.

The authors demonstrate here that **gp96** mols. contain ATP-binding cassettes, bind ATP and possess an Mg2+-dependent ATPase activity. **Gp96** prepns. are also obsd. to contain tightly **bound** peptides, which can be eluted by acid extn. These properties of **gp96** are consistent with its proposed roles in chaperoning **antigenic** peptides and in facilitating MHC class I-peptide assembly in the ER lumen. The authors present a model to explain how interaction of **gp96** with MHC class I may result in transfer of peptides to the latter.

L65 ANSWER 28 OF 32 MEDLINE
AN 93048763 MEDLINE
DN 93048763
TI [New perspectives in immunotherapy: adhesion molecules, superantigens, heat-shock proteins and cytokine antagonists]. Neue Perspektiven in der Immuntherapie: Adhasionsmolekule, Superantigene, Hitze-Schock-Proteine und Zytokinantagonisten.
AU Gause A; Sahin U; Pfreundschuh M
CS Abteilung Innere Medizin I, Universitat des Saarlandes, Homburg.
SO DEUTSCHE MEDIZINISCHE WOCHENSCHRIFT, (1992 Nov 13) 117 (46) 1764-73.
Ref: 59
Journal code: ECL. ISSN: 0012-0472.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
FS Priority Journals; Cancer Journals
EM 199302

L65 ANSWER 29 OF 32 MEDLINE
AN 92313999 MEDLINE
DN 92313999
TI Induction of arteriosclerosis in normocholesterolemic rabbits by immunization with heat shock protein 65.
AU Xu Q; Dietrich H; Steiner H J; Gown A M; Schoel B; Mikuz G; Kaufmann S H; Wick G
CS Institute for Biomedical Aging Research, Austrian Academy of Sciences, Innsbruck..
SO ARTERIOSCLEROSIS AND THROMBOSIS, (1992 Jul) 12 (7) 789-99.
Journal code: AZ1. ISSN: 1049-8834.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199210
AB Previous studies have established the presence of high numbers of activated T lymphocytes and "aberrant" expression of major histocompatibility **complex** class II antigens by endothelial and smooth muscle cells in human atherosclerotic lesions, implicating the involvement of a local cellular immune response. The identity of the antigen(s) eliciting this immune response, the extent of their effect, and the atherogenic stage at which they occur remain to be determined. In the present studies, 120 normocholesterolemic New Zealand White rabbits were immunized one or more times with various antigens, with or without adjuvants. The antigens and adjuvants included human or rabbit atherosclerotic lesion proteins, ovalbumin, Freund's complete and/or incomplete adjuvants, recombinant mycobacterial heat shock protein 65 (hsp65), and two hsp-free adjuvants, Ribi complete adjuvant and lipopeptide. In addition, some groups received a high-cholesterol diet. Sixteen weeks after the first immunization the animals were killed, and

arteriosclerotic lesions in the intima of the aortic arch were found to have developed only in those animals immunized with antigenic preparations containing hsp, either in the form of whole mycobacteria or as purified recombinant hsp65, although their serum cholesterol levels were normal. No arteriosclerotic changes exceeding those of controls were found in the other groups, irrespective of the antigen used. Immunohistopathologic examination revealed that the lesions contained 20% T cells, 10-30% macrophages, and 10-40% smooth muscle cells. Analysis of the peripheral blood T-lymphocyte proliferative responses revealed that the occurrence of lesions was positively correlated with the presence of hsp65-reactive T cells, suggesting that hsp65 is involved in the induction of arteriosclerotic lesions. Furthermore, combined immunization with hsp-containing material and a cholesterol-rich diet provoked development of significantly more severe atherosclerosis and the appearance of characteristic foam cells. We conclude that an (auto)immune response to hsp may initiate the development of atherosclerosis and that a high blood cholesterol level is only one albeit a very important risk factor.

L65 ANSWER 30 OF 32 CAPLUS COPYRIGHT 1999 ACS
AN 1992:53923 CAPLUS
DN 116:53923
TI Formation in vitro of **complexes** between an abnormal fusion protein and the **heat-shock** proteins from Escherichia coli and yeast mitochondria
AU Sherman, Michael Yu; Goldberg, Alfred L.
CS Dep. Cell. Mol. Physiol., Harvard Med. Sch., Boston, MA, 02115, USA
SO J. Bacteriol. (1991), 173(22), 7249-56
CODEN: JOBAAY; ISSN: 0021-9193
DT Journal
LA English
AB **Heat-shock** proteins (HSPs) of the Hsp70 and GroEL families assoc. with a variety of cell proteins in vivo. However, the formation of such **complexes** has not been systematically studied. A 31-kDa fusion protein (CRAG), which contains 12 residues of cro repressor, truncated protein A, and 14 residues of .beta.-galactosidase, when expressed in E. coli, was found in **complexes** with DnaK, GrpE, protease La and GroEL. When an E. coli ext. not contg. CRAG was applied to an affinity **column** contg. CRAG, DnaK, GroEL, and GrpE were selectively bound. These HSPs did not bind to a normal protein A **column**. DnaK, GrpE, and the fraction of GroEL could be eluted from the CRAG **column** with ATP but not with a **nonhydrolyzable** ATP analog. The ATP-dependent release of DnaK and GroEL also required Mg2+, but GrpE dissocd. with ATP alone. The binding and release of DnaK and GroEL were independent events, but the binding of GrpE required DnaK. Inactivation of DnaJ, GrpE, and GroES did not affect the assocn. or dissocn. of DnaK or GroEL from CRAG. The DnaK and GrpE proteins could be eluted with 10-6M ATP, but 10-4M was required for GroEL release. This approach allows a one-step purifn. of these proteins from E. coli and also the isolation of the DnaK and GroEL homologs from yeast mitochondria. Competition expts. with oligopeptide fragments of CRAG showed that DnaK and GroEL interact with different sites on CRAG and that the cro-derived domain of CRAG contains the DnaK-binding site.

L65 ANSWER 31 OF 32 MEDLINE
AN 92008132 MEDLINE
DN 92008132
TI Mycobacterial heat-shock proteins as carrier molecules.
AU Lussow A R; Barrios C; van Embden J; Van der Zee R; Verdini A S;

Pessi A; Louis J A; Lambert P H; Del Giudice G
CS World Health Organization-Immunology Research and Training Center, Department of Pathology, University of Geneva, Switzerland,.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1991 Oct) 21 (10) 2297-302. Journal code: EN5. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199201
AB We have previously shown that the priming of mice with live Mycobacterium tuberculosis var. bovis (Bacillus Calmette-Guerin, BCG) and immunization with the repetitive malaria synthetic peptide (NANP)40 conjugated to purified protein derivative (PPD), led to the induction of high and long-lasting titers of anti-peptide IgG antibodies, overcoming the requirement of adjuvants and the genetic restriction of the antibody response to the peptide (Lussow et al., Proc. Natl. Acad. Sci. USA 1990. 87:2960). This initial work led us to the following observations. BCG had to be live for priming to lead to the induction of anti-peptide antibodies. Surprisingly, priming with other living microorganisms which chronically infect the macrophage (e.g. Salmonella typhimurium and Leishmania major) also induced anti-peptide antibodies in mice immunized with PPD-(NANP)40 conjugate. It was, thus, hypothesized that molecules expressed during active infection and also known to be highly conserved between species, namely the heat-shock proteins (hsp), could mediate the T cell sensitization required for the production of anti-peptide antibodies. In fact, when the PPD protion of the conjugate was replaced by a highly purified recombinant protein corresponding to the 65-kDa (GroEL-type) hsp of M. bovis, this resulted in the production of anti-(NANP) IgG antibodies in BCG-primed mice, irrespective of the major histocompatibility **complex**-controlled responsiveness to the (NANP) sequence itself. Further, similar induction of anti-peptide antibody response was also obtained with a recombinant 70-kDa (DnaK-type) hsp of M. tuberculosis, but not with a small molecular mass (18 kDa) of M. leprae. Finally, an adjuvant-free carrier effect for anti-peptide IgG antibody production in BCG-primed mice, was also exerted by the GroEL hsp of Escherichia coli. This finding that hsp can act as carrier molecules without requiring conventional adjuvants is of potential importance in the development of vaccine strategies.

L65 ANSWER 32 OF 32 CAPLUS COPYRIGHT 1999 ACS
AN 1988:200399 CAPLUS
DN 108:200399
TI Purification of **complexes** of nuclear oncogene p53 with rat and Escherichia coli **heat shock** proteins: in vitro dissociation of hsc70 and dnaK from murine p53 by ATP
AU Clarke, Catherine F.; Cheng, Karen; Frey, Alan B.; Stein, Robert; Hinds, Philip W.; Levine, Arnold J.
CS Dep. Mol. Biol., Princeton Univ., Princeton, NJ, 08544, USA
SO Mol. Cell. Biol. (1988), 8(3), 1206-15 CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB Oligomeric protein **complexes** contg. the nuclear oncogene p53 and the simian virus 40 large tumor antigen, the adenovirus E1B 55-kilodalton (kDa) tumor antigen, and the **heat shock** protein hsc70 have all been previously described. To begin isolating, purifying, and testing these **complexes** for functional activities, a rapid immunoaffinity **column** purifn. procedure was developed. The p53-protein **complexes**

are eluted from the immunoaffinity **column** by using a molar excess of a peptide comprising the epitope recognized by the p53 monoclonal antibody. This mild and specific elution condition allows p53-protein interactions to be maintained. The hsc70-p53 **complex** from rat cells is heterogeneous in size, with some forms of this **complex** assocd. with a 110-kilodalton protein. The max. apparent mol. mass of such **complexes** is 660 kDa. Incubation with micromolar levels of ATP dissocs. this **complex** in vitro into p53 and hsc70 110-kDa components. **Nonhydrolyzable** substrates of ATP fail to promote this dissocn. of the **complex**. Murine p53 synthesized in Escherichia coli was purified 660-fold on the same antibody affinity **column** and was found to be assocd. with an E. coli protein of 70 kDa. Immunoblot anal. with specific antisera demonstrated that this E. coli protein was the **heat shock** protein dnaK, which has extensive sequence homol. with the rat hsc70 protein. Incubation of the immunopurified p53-dnaK **complex** with ATP resulted in the dissocn. of the p53-dnaK **complex** as it did with the p53-hsc70 **complex**. This remarkable conservation of p53-**heat shock** protein interactions and the specificity of dissocn. reactions suggest a functionally important role for **heat shock** proteins in their interactions with oncogene proteins.

FILE 'HOME' ENTERED AT 10:12:18 ON 06 JAN 1999

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? ds1-s17

Set     Items   Description
S1      22525   HEAT(W)SHOCK(W)PROTEIN?
S2       3749   S1(W)(70 OR 90)
S3       9020   HSP70 OR HSP90 OR HSP(W)(70 OR 90)
S4        121   GP96 OR GP(W)96
S5    1186784   COMPLEX? OR BOUND
S6         63   S1(S)S4
S7       1908   (S2 OR S3 OR S6) (S)S5
S8      99283   ANTIGENIC?
S9         38   S7(S)S8
S10      4815   NONHYDROLY? OR NON(W)HYDROLY?
S11        21   S10 AND (S2 OR S3)
S12      1890   S7 AND (S2 OR S3)
S13        16   S7 AND S10
S14         9   RD (unique items)
S15    176619   IMMUNOSTIMUL? OR IMMUNE(W)RESPONS?
S16     28105   IMMUNOMODULAT?
S17        10   S9 AND (S15 OR S16)
? s s13 or s17

            16  S13
            10  S17
     S20    26  S13 OR S17
? rd

>>>Duplicate detection is not supported for File 347.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S21    16  RD (unique items)
? t s21/7/1-16


 21/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:BIOSIS PREVIEWS(R)
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11514439   BIOSIS NO.: 199800295771
Heat shock protein 70 regulation is related to HLA-DR expression in
  bronchial asthma: Effects of inhaled glucocorticoids.

AUTHOR: Bertorelli G(a); Bocchino V; Zhuo X; Chetta A; Del Donno M; Foresi
  A; Testi R; Olivieri D
AUTHOR ADDRESS: (a)Dep. Respiratory Dis., Univ. Parma, Rasori Hosp., Via
  Rosari 10, 43100 Parma, Italy

JOURNAL: Clinical and Experimental Allergy  28 (5):p551-560 May, 1998
ISSN: 0954-7894
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background and Objective. Antigen processing determines the
  production of peptides from antigens - including allergens - and their
  binding to class II major histocompatibility complex molecules, that
  stimulate T-cell responses. Heat shock protein (****hsp****) ****70****
  are recognized to have a role in chaperoning ****antigenic**** peptides
  and in facilitating class 11 peptide assembly. We studied the HLA-DR and
  ****hsp70**** expression on BAL cells and bronchial biopsies from
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MEDLINE UPDATES ON HOLD UNTIL AFTER THE ANNUAL RELOAD HAS BEEN COMPLETED. NOTICE WILL BE GIVEN ONCE THE RELOAD IS COMPLETED AND RELOAD DETAILS WILL BE FOUND IN HELP RLOAD.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

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L28         1786 SEA FILE=MEDLINE ABB=ON  HEAT-SHOCK PROTEINS 70/CT
L29           76 SEA FILE=MEDLINE ABB=ON  L28(L)IP/CT - Subheading - Isolation & purification
L30       320141 SEA FILE=MEDLINE ABB=ON  CHROMATOGRAPHY+NT/CT
L31           35 SEA FILE=MEDLINE ABB=ON  L29 AND L30
L32         2143 SEA FILE=MEDLINE ABB=ON  NON HYDROLY? OR NONHYDROLY?
L33            1 SEA FILE=MEDLINE ABB=ON  L31 AND L32


L28         1786 SEA FILE=MEDLINE ABB=ON  HEAT-SHOCK PROTEINS 70/CT
L29           76 SEA FILE=MEDLINE ABB=ON  L28(L)IP/CT -
L30       320141 SEA FILE=MEDLINE ABB=ON  CHROMATOGRAPHY+NT/CT
L31           35 SEA FILE=MEDLINE ABB=ON  L29 AND L30
L34        56199 SEA FILE=MEDLINE ABB=ON  ADENOSINE TRIPHOSPHATE+NT/CT
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L25        10392 SEA FILE=MEDLINE ABB=ON  HEAT-SHOCK PROTEINS+NT/CT
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L41       326137 SEA FILE=MEDLINE ABB=ON  COMPLEX?
L43        26958 SEA FILE=MEDLINE ABB=ON  IMMUNIZATION/CT
L44        12502 SEA FILE=MEDLINE ABB=ON  ADJUVANTS, IMMUNOLOGIC/CT
L47          954 SEA FILE=MEDLINE ABB=ON  L26(L)IM/CT - Subheading - Immunology
L49        12350 SEA FILE=MEDLINE ABB=ON  IMMUNOTHERAPY/CT
L50        19630 SEA FILE=MEDLINE ABB=ON  L43/MAJ OR L44/MAJ OR L49/MAJ
L51            7 SEA FILE=MEDLINE ABB=ON  L47 AND L41 AND L50


L64           16 L33 OR L35 OR L51

=> fil wpids; d que l57; d que l60
FILE 'WPIDS' ENTERED AT 10:11:18 ON 06 JAN 1999
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FILE LAST UPDATED: 23 DEC 1998              <19981223/UP>
>>>UPDATE WEEKS:
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DERWENT WEEK FOR CHEMICAL CODING:   199846
DERWENT WEEK FOR POLYMER INDEXING:  199848
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> D COST AND SET NOTICE DO NOT REFLECT SUBSCRIBER DISCOUNTS -
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>>> INDEXING UPDATE CODES JUMP FORWARD TO 9901   -  SEE NEWS <<<


L52          176 SEA FILE=WPIDS ABB=ON  HEAT SHOCK PROTEIN#
L53           18 SEA FILE=WPIDS ABB=ON  GP90 OR GP96 OR GP70
L54       447007 SEA FILE=WPIDS ABB=ON  90 OR 96 OR 70
L55           32 SEA FILE=WPIDS ABB=ON  L52 AND (L53 OR L54)
L56       146763 SEA FILE=WPIDS ABB=ON  COMPLEX? OR BOUND
L57            6 SEA FILE=WPIDS ABB=ON  L55 AND L56
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Searched by Barb O'Bryen, STIC 308-4291

21/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11042220 BIOSIS NO.: 199799663365
Generation of heat shock protein-based vaccines by intracellular loading of gp96 with antigenic peptides.

AUTHOR: Heikema Astrid(a); Agsteribbe Etienne; Wilschut Jan; Huckriede Anke
AUTHOR ADDRESS: (a)Dep. Physiological Chem., Univ. Groningen, A. Deusinglaan 1, NL-9713 AV Groningen, Netherlands

JOURNAL: Immunology Letters 57 (1-3):p69-74 1997
ISSN: 0165-2478
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Several studies have shown that immunization with heat shock proteins (HSPs) purified from tumors of virus-infected cells induces specific cytotoxic T-cell (CTL) activity. This ****immune**** ****response**** is directed against peptides ****bound**** to the HSPs rather than against the HSPs themselves. The peptides are derived from tumor- or virus-specific proteins which are degraded in the course of normal protein turnover and processing for presentation by MHC class I molecules. The HSPs appear to function as carriers for the ****antigenic**** peptides. Upon immunization they ensure their uptake by specialized macrophages and their introduction into the MHC class I presentation route which is otherwise accessible only for intracellular proteins. Using influenza virus nucleoprotein (NP) as a model antigen, we have tested whether an HSP-based vaccine can be produced by overexpressing an antigen in cultured cells prior to purification of the HSP's. The transfection system based on the Semliki Forest virus (SFV) replicon was employed to achieve high expression of NP. Since SFV-mediated transfection of murine cells was inefficient we used the hamster-derived cell line BHK21, which can be transfected with 100% efficiency, as a source for NP peptide-loaded ****gp96****. The protein was purified from transfected cells and used for first vaccination studies. The hamster ****gp96**** preparation was well tolerated in mice, an antibody response against the foreign protein was not observed. Preliminary results suggest that a cellular ****immune**** ****response**** against NP was indeed induced. SFV transfection is applicable for any known antigen and is therefore considered to be an elegant means for the production of HSP-based vaccines capable of inducing a cellular ****immune**** ****response****.

21/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

10691616 BIOSIS NO.: 199799312761
The second step of ATP binding of DnaK induces peptide release.

AUTHOR: Theyssen Holger; Schuster Hans-Peter; Packschies Lars; Bukau Bernd; Reinstein Jochen(a)
AUTHOR ADDRESS: (a)Max-Planck-Inst. Mol. Physiol., Abt. Physikalische Biochemie, Rheinlanddamm 201, D-44139 Dortmun, Germany

JOURNAL: Journal of Molecular Biology 263 (5):p657-670 1996
ISSN: 0022-2836
RECORD TYPE: Abstract

fragments and derivs. thereof. In a preferred embodiment, the **complex** is autologous to the individual. In a specific embodiment, the effective amts. of the **complex** are in the range of 0.1 to 9.0 .mu.g for **complexes** comprising hsp70, 5 to 49 .mu.g, for hsp90, and 0.1 to 9.0 .mu.g for **gp96**.

L65 ANSWER 2 OF 32 CAPLUS COPYRIGHT 1999 ACS
AN 1998:548557 CAPLUS
DN 129:156934
TI Adoptive immunotherapy utilizing **heat shock** /stress protein-peptide **complexes** for prevention/treatment of cancer or infectious diseases
IN Srivastava, Pramod K.
PA Fordham University, USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9834642	A1	19980813	WO 98-US2194	19980203
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GW, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5830464	A	19981103	US 97-796316	19970207
	AU 9860564	A1	19980826	AU 98-60564	19980203
PRAI	US 97-796316	19970207			
	WO 98-US2194	19980203			

AB Methods and compns. are provided for eliciting an immune response and the prevention and treatment of primary and metastatic neoplastic diseases and infectious diseases. The methods of the invention comprise administering a compn. comprising an effective amt. of a **complex**, in which the **complex** consists essentially of a **heat shock** protein (hsp) noncovalently **bound** to an **antigenic** mol. in combination with administering antigen-presenting cells sensitized with **complexes** of hsps noncovalently **bound** to an **antigenic** mol. "**Antigenic** mol." as used herein refers to the peptides with which the hsps are endogenously assocd. in vivo as well as exogenous antigens/immunogens (i.e., with which the hsps are not **complexed** in vivo) or **antigenic** /immunogenic fragments and derivs. thereof. In a preferred embodiment, the **complex** is autologous to the individual. In a specific embodiment, the effective amts. of the **complex** when administered intradermally are in the range of 0.1 to 9.0 .mu.g for **complexes** comprising hsp70, 5 to 49 .mu.g for hsp90, and 0.1 to 9.0 .mu.g for **gp96**. In another embodiment, the effective amts. of the **complex** when administered s.c. are in the range of 10 to 600 .mu.g for **complexes** comprising hsp70, 50 to 5000 .mu.g for hsp90, and 10 to 600 .mu.g for **gp96**.

L65 ANSWER 3 OF 32 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 98-168893 [15] WPIDS
DNC C98-054070
TI Vaccine for treatment of auto-immune disease prepared from patient's

ABSTRACT: Interaction of preproteins with the heat shock protein ****Hsp70**** in the mitochondrial matrix is required for driving protein transport across the mitochondrial inner membrane. Binding of mt-****Hsp70**** to the protein Mim44 of the inner membrane import site seems to be an essential part of an ATP-dependent reaction cycle. However, the available results on the role played by ATP are controversial. Here we demonstrate that the mt-****Hsp70****-Mim44 ****complex**** contains ADP and that a ****nonhydrolyzable**** analog of ATP dissociates the mt-****Hsp70****-Mim44 ****complex**** in the presence of potassium ions. The previously reported requirement of ATP hydrolysis for ****complex**** dissociation was due to the use of a nonphysiological concentration of sodium ions. In the presence of potassium ions, mt-****Hsp70**** undergoes a conformational change that is not observed with a mutant ****Hsp70**** defective in binding to Mim44. The mutant ****Hsp70**** is able to bind substrate proteins, differentiating binding to Mim44 from binding to substrate proteins. We conclude that binding of ATP, not hydrolysis, is required to dissociate the mt-****Hsp70****-Mim44 ****complex**** and that the reaction cycle includes an ATP-induced conformational change of mt-****Hsp70****.

21/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09903228 BIOSIS NO.: 199598358146
Binding of p23 and hsp90 during Assembly with the Progesterone Receptor.

AUTHOR: Johnson Jill L; Toft David O(a)
AUTHOR ADDRESS: (a)Dep. Biochem. Mol. Biol., Mayo Grad. Sch., Rochester, MN 55905, USA

JOURNAL: Molecular Endocrinology 9 (6):p670-678 1995
ISSN: 0888-8809
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Upon incubation in rabbit reticulocyte lysate, the unactivated progesterone receptor (PR) associates with the heat shock proteins ****hsp90**** and ****hsp70****, the immunophilins FKBP52, FKBP54, and CyP-40, and another protein p23. We have previously described a protein ****complex**** between p23, ****hsp90****, and the immunophilins that forms in rabbit reticulocyte lysate in the absence of the PR. Immunodepletion of p23 from lysate prevented the binding of ****hsp90**** and CyP-40 to the PR, suggesting that ****hsp90****, CyP-40, and p23 bind the receptor as a ****complex****. We have further examined the properties of this p23 ****complex**** to determine how it is involved in receptor assembly in vitro. Use was made of three chemical probes, sodium molybdate, the ****nonhydrolyzable**** ATP analog, 5'-adenylylimidodiphosphate, and the ****hsp90****-binding agent geldanamycin. Molybdate has previously been shown to stabilize the heat-induced dissociation of ****hsp90**** and p23 from the PR. This stabilization is not mediated through the PR, as molybdate stabilizes the heat-induced dissociation of ****hsp90**** from p23 even in the absence of the PR. Molybdate also stabilizes both p23 and PR ****complexes**** under conditions of low ATP and magnesium concentration. The ATP analog, 5'-adenylylimidodiphosphate, which does not support the assembly of PR ****complexes****, promotes both the assembly and stabilization of p23 ****complexes****. Geldanamycin disrupts p23 ****complexes****, and when PR ****complexes**** are treated with this agent, p23, CyP-40, and some ****hsp90**** are lost from the receptor. Thus, all three of these

The immunization capacity of HSP relies on their ability to bind **antigenic** peptides. The authors show that HSP70 and **gp96** prepns. purified from the ovalbumin (OVA)-transfected cell line E.G7 are assocd. with processed H-2Kb-binding peptides which contain the major H-2Kb-assocd. epitope SIINFEKL (OVA257-264). The data show for the 1st time in the well-defined OVA antigen system that not only endoplasmic reticulum-resident HSP, like **gp96**, are assocd. with processed **antigenic** peptides but that also the cytosolic HSP70 protein forms **complexes** with major finally processed MHC-binding epitopes.

L65 ANSWER 5 OF 32 MEDLINE
AN 1998172711 MEDLINE
DN 98172711
TI Interaction of heat stress glycoprotein GP50 with classical heat-shock proteins.
AU Jethmalani S M; Henle K J
CS Department of Medicine, University of Arkansas for Medical Sciences, Little Rock 72205-5484, USA.
NC CA-33405 (NCI)
SO EXPERIMENTAL CELL RESEARCH, (1998 Feb 25) 239 (1) 23-30.
Journal code: EPB. ISSN: 0014-4827.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199806
EW 19980602
AB Cellular stress conditions are known to elevate heat-shock protein (HSP) synthesis and protein glycosylation, leading to the development of cellular thermotolerance. In the present study, we investigated the interaction of a major stress glycoprotein, GP50, with other cellular proteins during recovery from heat stress, using' mostly immunoprecipitation techniques. Parallel studies of heat-stressed CHO and M21 cells showed that both glycosylated and unglycosylated forms of GP50 interact with several members of the classical HSP families (e.g., HSP70 and HSP90) in an ATP-dependent manner. The specificity of HSP-stress glycoprotein interactions was confirmed by chemical crosslinking with a homobifunctional agent, 3,3'-dithiobis (succinimidyl propionate). Interaction of GP50 with denatured proteins was also demonstrated through binding to gelatin. Protein complexes formed between stress glycoproteins and HSPs were further characterized by gel filtration and showed an average molecular mass between 400 and 600 kDa. Overall, the consistent association of stress glycoproteins with nonglycosylated HSPs suggests a structural/functional role for protein chaperone complexes that consist of denatured proteins and the glycone/aglycone elements of cellular stress response.

L65 ANSWER 6 OF 32 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 2
AN 1997:299378 CAPLUS
DN 126:272363
TI Treatment or prevention of neoplastic and infectious diseases with immune response-augmenting **heat shock**/stress protein **complexes**, method for measuring tumor rejection, and **heat shock** protein 70-peptide **complex** purification
IN Srivastava, Pramod K.
PA Fordham University, USA
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent

LANGUAGE: English

ABSTRACT: We characterized a 24-kDa protein associated with matrix ****hsp70**** (mt-****hsp70****) of Neurospora crassa and Saccharomyces cerevisiae mitochondria. By using specific antibodies, the protein was identified as MGE, a mitochondrial homolog of the prokaryotic heat shock protein GrpE. MGE extracted from mitochondria was quantitatively ****bound**** to ****hsp70****. It was efficiently released from ****hsp70**** by the addition of Mg-ATP but not by ****nonhydrolyzable**** ATP analogs or high salt. A mutant mt-****hsp70****, which was impaired in release of ****bound**** precursor proteins, released MGE in an ATP-dependent manner, indicating that precursor proteins and MGE bind to different sites of ****hsp70****. A preprotein accumulated in transit across the mitochondrial membranes was specifically coprecipitated by either antibodies directed against MGE or antibodies directed against mt-****hsp70****. The preprotein accumulated at the outer membrane was not coprecipitated by either antibody preparation. After being imported into the matrix, the preprotein could be coprecipitated only by antibodies against mt-****hsp70****. We propose that mt-****hsp70**** and MGE cooperate in membrane translocation of preproteins.

21/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

09191360 BIOSIS NO.: 199497199730
Heat stress induces hsc70/nuclear topoisomerase I complex formation in vivo: Evidence for hsc70-mediated, ATP-independent reactivation in vitro.

AUTHOR: Ciavarra Richard P(a); Goldman Charles; Wen Kuo-Kuang; Tedeschi Bruce; Castora Frank J
AUTHOR ADDRESS: (a)Dep. Microbiol., Eastern Virginia Med. Sch., Norfolk, VA 23501, USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 91 (5):p1751-1755 1994
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We previously demonstrated that in murine T cells thermotolerance correlated with heat shock protein 70 (****hsp70****) synthesis and protection of nuclear type I topoisomerase (topo I). Topo I activity returned to normal levels following heat stress even in cells not rendered thermotolerant by a prior heat shock. Recovery of topo I activity was not dependent on de novo protein synthesis, suggesting that the cell possesses a pathway(s) for refolding this nuclear protein. In this report we demonstrate that topo I and hsc70, the constitutively produced member of the ****hsp70**** family, associated in vivo during heat stress. That this association may play a physiologically important role in protecting topo I activity from heat stress was suggested by the observation that hsc70 protected topo I from heat inactivation in vitro. hsc70 but not actin also reactivated previously heat-denatured topo I in a dose-dependent fashion. However, refolding of heat-denatured topo I by purified hsc70 was inefficient relative to a hsc70-containing cell lysate. Protection from heat inactivation as well as reactivation by hsc70 did not require exogenous ATP. Similarly, reactivation by the cell lysate was not inhibited by ADP or a ****nonhydrolyzable**** analogue of ATP. Thus, our studies suggest that nuclear topo I ****complexes**** with

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9669735	A1	19970401	AU 96-69735	19960911
EP 857068	A1	19980812	EP 96-930819	19960911

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI US 95-527546 19950913
WO 96-US14558 19960911

AB Methods and compns. are disclosed for enhancing immunol. responses and for the prevention and treatment of infectious diseases or primary and metastatic neoplastic diseases based on the administration of macrophages and/or other antigen-presenting cells (APC) sensitized with **heat-shock** proteins noncovalently **bound** to peptide **complexes** and/or **antigenic** components. APC are incubated in the presence of hsp-peptide **complexes** and/or **antigenic** components in vitro. The **heat-shock** protein may be e.g. hsp70, hsp90, or **gp96**. Macrophages sensitized with **gp96** isolated from N1 cells (EL4 cells transfected with the gene encoding nucleocapsid protein VS1) were lysed by vesicular stomatitis virus-specific cytotoxic T-lymphocytes, while those sensitized with **gp96** from untransfected EL4 cells were not.

L65 ANSWER 8 OF 32 CAPLUS COPYRIGHT 1999 ACS
AN 1997:254287 CAPLUS
DN 126:233701
TI Therapeutic and prophylactic methods using **heat shock** protein-antigen **complexes** to elicit immune responses
IN Srivastava, Pramod K.
PA Fordham University, USA
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9710000	A1	19970320	WO 96-US14556	19960911

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, FI, GE, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9669734	A1	19970401	AU 96-69734	19960911
EP 851765	A1	19980708	EP 96-930818	19960911

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRAI US 95-527547 19950913
US 96-711918 19960910
WO 96-US14556 19960911

AB Immunogenic **complexes** of **heat shock** proteins (hsp) noncovalently bound to exogenous antigenic mols. are disclosed which, when administered to an individual, elicit specific immunol. responses in the host. Methods and compns. for prevention and treatment of cancer and infectious disease are provided. An hsp70-ovalbumin **complex** induced a far grater cytotoxic T-lymphocyte response than either hsp70 alone or ovalbumin alone.

NORTHWESTERN UNIVERSITY, EVANSTON, ILL. 60208.

JOURNAL: GENES DEV 6 (7). 1992. 1153-1164.
FULL JOURNAL NAME: Genes & Development
CODEN: GEDEE
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Transcriptional regulation of the human ****hsp70**** gene in response to heat shock and other forms of physiological stress occurs through the activation of heat shock transcription factor (HSF). Exposure of cells to a heat shock temperature of 42.degree. C results in transient activation of HSF; its DNA-binding activity increases rapidly, plateaus, and attenuates, during which the intracellular levels of ****hsp70**** increase. In an effort to understand whether HSF is regulated negatively by ****hsp70****, we have examined whether HSF associates with ****hsp70****. We show that activated HSF associates with ****hsp70**** and that the interaction is detected as the levels of ****hsp70**** increase in the cell. Addition of ATP and other hydrolyzable nucleotides results in the dissociation of ****hsp70**** from HSF while ****nonhydrolyzable**** nucleotide analogs do not disrupt the ****complex****. We demonstrate that exogenous recombinant wild-type ****hsp70**** can associate with activated HSF, whereas no association is observed with an amino-terminal or a carboxy-terminal deletion mutant of ****hsp70****. We also show that ****hsp70**** blocks the in vitro activation of HSF from its cryptic non-DNA-binding state to a DNA-binding from; this inhibitory effect of ****hsp70**** is abolished by aTP. We sugegst that ****hsp70**** may negatively regulate the activation of HSF.

21/7/12 (Item 12 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

07969264 BIOSIS NO.: 000093036842
FORMATION IN-VITRO OF COMPLEXES BETWEEN AN ABNORMAL FUSION PROTEIN AND THE HEAT SHOCK PROTEINS FROM ESCHERICHIA-COLI AND YEAST MITOCHONDRIA

AUTHOR: SHERMAN M YU; GOLDBERG A L
AUTHOR ADDRESS: DEP. CELL. AND MOL. PHYSIOL., HARVARD MED. SCH., BOSTON, MASS. 02115.

JOURNAL: J BACTERIOL 173 (22). 1991. 7249-7256.
FULL JOURNAL NAME: Journal of Bacteriology
CODEN: JOBAA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Heat shock proteins (HSPs) of the ****Hsp70**** and GroEL families associate with a variety of cell proteins in vivo. However, the formation of such ****complexes**** has not been systematically studied. A 31-kDa fusion protein (CRAG), which contains 12 residues of cro repressor, truncated protein A, and 14 residues of .beta.-galactosidase, when expressed in Escherichia coli, was found in ****complexes**** with DnaK, GrpE, protease La, and GroEL. When an E. coli extract not containing CRAG was applied to an affinity column containing CRAG, DnaK, GroEL, and GrpE were selectively ****bound****. These HSPs did not bind to a normal protein A column. DnaK, GrpE, and the fraction of GroEL could be eluted from the CRAG column with ATP but not with a ****nonhydrolyzable**** ATP analog. The ATP-dependent release of DnaK and GroEL also required Mg2+, but GrpE dissociated with ATP alone. The binding and release of DnaK and GroEL were independent events, but the

protein preparations derived from cancers other than the autologous cancer did not provide significant protection. Spontaneous cancers (lung cancer and melanoma), chemically induced cancers (fibrosarcoma and colon carcinoma), and an ultraviolet radiation-induced spindle cell carcinoma were tested, and the results support the efficacy of autologous cancer-derived heat shock protein-peptide **complexes** in immunotherapy of cancers without the need to identify specific tumor antigenic epitopes.

L65 ANSWER 11 OF 32 CAPLUS COPYRIGHT 1999 ACS
AN 1997:479409 CAPLUS
DN 127:189375
TI Generation of heat shock protein-based vaccines by intracellular loading of gp96 with antigenic peptides
AU Heikema, Astrid; Agsteribbe, Etienne; Wilschut, Jan; Huckriede, Anke
CS Department Physiological Chemistry, University Groningen, Groningen, 9713 AV, Neth.
SO Immunol. Lett. (1997), 57(1-3), 69-74
CODEN: IMLED6; ISSN: 0165-2478
PB Elsevier
DT Journal
LA English
AB Several studies have shown that immunization with **heat shock** proteins (HSPs) purified from tumors of virus-infected cells induces specific cytotoxic T-cell (CTL) activity. This immune response is directed against peptides **bound** to the HSPs rather than against the HSPs themselves. The peptides are derived from tumor- or virus-specific proteins which are degraded in the course of normal protein turnover and processing for presentation by MHC class I mols. The HSPs appear to function as carriers for the **antigenic** peptides. Upon immunization they ensure their uptake by specialized macrophages and their introduction into the MHC class I presentation route which is otherwise accessible only for intracellular proteins. Using influenza virus nucleoprotein (NP) as a model antigen, the authors tested whether an HSP-based vaccine can be produced by overexpressing an antigen in cultured cells prior to purifn. of the HSP. The transfection system based on the Semliki Forest virus (SFV) replicon was employed to achieve high expression of NP. Since SFV-mediated transfection of murine cells was inefficient the authors used the hamster-derived cell line BHK21, which can be transfected with 100% efficiency, as a source for NP peptide-loaded **gp96**. The protein was purified from transfected cells and used for first vaccination studies. The hamster **gp96** prepn. was well tolerated in mice, an antibody response against the foreign protein was not obsd. Preliminary results suggest that a cellular immune response against NP was indeed induced. SFV transfection is applicable for any known antigen and is therefore considered to be an elegant means for the prodn. of HSP-based vaccines capable of inducing a cellular immune response.

L65 ANSWER 12 OF 32 MEDLINE
AN 97346285 MEDLINE
DN 97346285
TI Purification of immunogenic heat shock protein 70-peptide complexes by ADP-affinity chromatography.
AU Peng P; Menoret A; Srivastava P K
CS Center for Immunotherapy of Cancer and Infectious Diseases, University of Connecticut School of Medicine, Farmington 06030, USA.
NC CA64394 (NCI)
CA44786 (NCI)
SO JOURNAL OF IMMUNOLOGICAL METHODS, (1997 May 12) 204 (1) 13-21.

21/7/14 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

10209871 EMBASE No: 97007932
Delayed-type hypersensitivity elicited by synthetic peptides complexed with Mycobacterium tuberculosis hsp 70
Roman E.; Moreno C.
Dr. C. Moreno, MRC Tuberculosis Unit, Clinical Sciences Centre, Royal Postgraduate Medical School, London W12 0NN United Kingdom
Immunology (United Kingdom) , 1997, 90/1 (52-56)
CODEN: IMMUA ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGES: English SUMMARY LANGUAGES: English
NUMBER OF REFERENCES: 22
Four synthetic peptides bearing dominant CD4+ T-cell epitopes of the 19,000 and 38,000 MW proteins of Mycobacterium tuberculosis were used to provoke a delayed-type hypersensitivity (DTH) reaction in mice previously immunized with recombinant 19,000 and 38,000 MW proteins. It was found that an effective enhancement of the DTH reaction was obtained if the peptides were administered as a complex with M tuberculosis ****hsp**** ****70**** protein. The increase in reactivity was not obtained when ****hsp**** ****70**** and peptide were co-injected at the same site, but not in ****complex****, or when the specific peptide was displaced from the ****complex**** by an irrelevant peptide with high capacity to bind ****hsp**** ****70****. One of the ****antigenic**** peptides whose capacity to ****complex**** with ****hsp**** ****70**** is low, failed to show the enhancement of DTH when injected together with ****hsp**** ****70****.

21/7/15 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

9819751 EMBASE No: 96000406
The mitochondrial protein import machinery. Role of ATP in dissociation of the ****Hsp70****.Mim44 ****complex****
Von Ahsen O.; Voos W.; Henninger H.; Pfanner N.
Biochemisches Institut, Universitat Freiburg, Hermann-Herder-Strasse 7, D-79104 Freiburg Germany
Journal of Biological Chemistry (USA) , 1995, 270/50 (29848-29853)
CODEN: JBCHA ISSN: 0021-9258
LANGUAGES: English SUMMARY LANGUAGES: English
Interaction of preproteins with the heat shock protein ****Hsp70**** in the mitochondrial matrix is required for driving protein transport across the mitochondrial inner membrane. Binding of mt-****Hsp70**** to the protein Mim44 of the inner membrane import site seems to be an essential part of an ATP-dependent reaction cycle. However, the available results on the role played by ATP are controversial. Here we demonstrate that the mt-****Hsp70****.Mim44 ****complex**** contains ADP and that a ****nonhydrolyzable**** analog of ATP dissociates the mt-****Hsp70****.Mim44 ****complex**** in the presence of potassium ions. The previously reported requirement of ATP hydrolysis for ****complex**** dissociation was due to the use of a nonphysiological concentration of sodium ions. In the presence of potassium ions, mt-****Hsp70**** undergoes a conformational change that is not observed with a mutant ****Hsp70**** defective in binding to Mim44. The mutant ****Hsp70**** is able to bind substrate proteins, differentiating binding to Mim44 from binding to substrate proteins. We conclude that binding of ATP, not hydrolysis, is required to dissociate the mt-****Hsp70****.Mim44 ****complex**** and that the reaction cycle includes an ATP-induced conformational change of mt-****Hsp70****.

L65 ANSWER 14 OF 32 CAPLUS COPYRIGHT 1999 ACS
AN 1996:367057 CAPLUS
DN 125:55699
TI Isolation of an immunodominant viral peptide that is endogenously bound to the stress protein GP96/GRP94
AU Nieland, Thomas J. F.; Tan, M. C. Agnes A.; Monnee-van Muijen, Monique; Koning, Frits; Kruisbeek, Ada M.; van Bleek, Grada M.
CS Div. Immunol., Netherlands Cancer Inst., Amsterdam, Neth.
SO Proc. Natl. Acad. Sci. U. S. A. (1996), 93(12), 6135-6139
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB **Heat shock** protein **gp96** primes class I restricted cytotoxic T cells against antigens present in the cells from which it was isolated. Moreover, **gp96** derived from certain tumors functions as an effective vaccine, causing complete tumor regressions in in vivo tumor challenge protocols. Because tumor-derived **gp96** did not differ from **gp96** isolated from normal tissues, a role for **gp96** as a peptide carrier has been proposed. To test this hypothesis, we analyzed whether such an assocn. of **antigenic** peptides with **gp96** occurs in a well-defined viral model system. Here we present the full characterization of an **antigenic** peptide that endogenously assocs. with the stress protein **gp96** in cells infected with vesicular stomatitis virus (VSV). This peptide is identical to the immunodominant peptide of VSV, which is also naturally presented by H-2Kb major histocompatibility **complex** class I mols. This peptide assocs. with **gp96** in VSV-infected cells regardless of the major histocompatibility **complex** haplotype of the cell. Our observations provide a biochem. basis for the vaccine function of **gp96**.

L65 ANSWER 15 OF 32 MEDLINE
AN 96351180 MEDLINE
DN 96351180
TI ATPase activity and molecular chaperone function of the stress70 proteins.
AU Miernyk J A; Hayman T G
CS National Center for Agricultural Utilization Research, Peoria, Illinois 61604, USA.. miernykj@ncaurl.ncaur.gov
SO PLANT PHYSIOLOGY, (1996 Feb) 110 (2) 419-24.
Journal code: P98. ISSN: 0032-0889.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
AB The codons for the amino acid residues making up the proposed ATP-binding sites of the maize (Zea mays L.) endoplasmic reticulum and tomato (Lycopersicon esculentum) cytoplasmic Stress70 proteins were deleted from their respective cDNAs. The deletions had little effect on the predicted secondary structure characteristics of the encoded proteins. Both wild-type and mutant proteins were expressed in Escherichia coli and purified to electrophoretic homogeneity. The mutant recombinant proteins did not bind to immobilized ATP columns, had no detectable ATPase activity, and were unable to function in vitro as molecular chaperones. Additionally, the inability to bind ATP was associated with changes in the oligomerization state of the Stress70 proteins.

L65 ANSWER 16 OF 32 WPIDS COPYRIGHT 1999 DERWENT INFORMATION LTD